Applicant : David E. Wolf   Attorney's Docket No.: 04037-011002
Serial No. : 10/706,687
Filed   : November 12, 2003
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REMARKS

Claims 1-21 are pending. All claims have been rejected.

Based on the rejections, applicant has the following general comments regarding polymers:

In a typical polymer production process, feedstock materials are combined together under reaction conditions to form a polymer. These polymers are formed by reacting molecules together in competing reactions. The random nature of the process naturally produces polymer chains having a range of molecular weights. The polymers are referred to as polymers of a certain molecular weight (or number), even though one of skill in the art understands that the weight (or number) used only refers to a weight average (or number average) of the polymer chains, and that in reality there is a broad range of polymer chain lengths present. Therefore, even if a polymer is referred to as a polymer having a molecular weight of, for example, 15,000 – one of skill in the art understands that the polymer inherently includes polymer chains having a range of molecular weights (typically having a Gaussian distribution), with an average molecular weight of 15,000. An article is attached providing additional background information.

In contrast, producing a monodisperse polymer requires specialized reaction or processing conditions to ensure the proper conditions for producing a narrow range of polymer chain lengths. This range is much narrower than the typical polymeric range discussed above, and the polymer formed using such a process will be referred to as a monodisperse polymer to distinguish it from the usual polymer nomenclature.

With this in mind, we turn to the rejections.

§112 Rejections

Claims 1-21 have been rejected under 35 U.S.C. §112, first paragraph. The rejection appears to be based on Examples 1 and 2 showing the polymer being added to a solution for coating. Although the monodisperse polymer is added to a liquid in Examples 1 and 2, the polymer does not change from being a monodisperse polymer. A monodisperse polymer refers

to a polymer having a narrow range of chain lengths. In the described solutions, there are no reactions that change the state of the polymer from being a monodisperse polymer.

Claims 1-14, 16, and 18-21 have been rejected under 35 U.S.C. §112, first paragraph on the ground of not enabling a coated aqueous solution. The rejection appears based on the language of claim 18, which recites (in pertinent part) "wherein said core comprises an aqueous solution." There are many options for a core comprising an aqueous solution including, for example, microcapsules, a solution within a gel, a solution surrounded by a gel, etc. Such approaches are well known in the art – for example, solutions in a core are referred to in the cited references, and are shown, for example, in Example 1 (islet) and Example 2 (microsphere sensor beads) of the current application.

Claims 1-21 have been rejected under 35 U.S.C. §112, second paragraph as indefinite on the ground that it is unclear whether the monodisperse polymer is directed to the coating on a core or an article itself. Based on the claim language, "said coating comprising a monodisperse polymer," it is clear that the coating comprises a monodisperse polymer.

Applicant therefore requests withdrawal of all §112 rejections.

Double Patenting

Claims 1-16 and 19-21 have been rejected for non-statutory obviousness-type double patenting over claims 12-26 and 31-82 of Lanza et al., U.S. Patent No. 6,126,936 ("Lanza").

As discussed below, Lanza does not teach, describe, or suggest the use of a monodisperse polymer. Thus, the pending claims are not co-extensive, and are not obvious in view of Lanza. Accordingly, applicant requests reconsideration and withdrawal of the double patenting rejection.

Claim Rejections

Claims 1-3, 5-6, 8-11, 13-16, and 19-21 have been rejected under 35 U.S.C. §102(b), or alternatively under 35 U.S.C. §103(a), over Goosen et al., U.S. Patent No. 4,806,355 ("Goosen"), and claims 1-16 and 19-21 have been rejected under 35 U.S.C. §103(a) over Goosen. Goosen

describes the microencapsulation of living tissue or cells using a biocompatible semi-permeable membrane, with a negatively charged outer surface. The membrane is formed from cross-linking biocompatible polymers having a molecular weight that may vary widely (typically in the range of 11,000 to about 4,000,000).

Claims 1-2, 5, 8-11, 13-16, and 19-21 have been rejected under 35 U.S.C. §102(b), or under 35 U.S.C. §103(a), over Weber et al., U.S. Patent No. 5,227,298 ("Weber"). Weber describes a method for encapsulation of tissue or cells within a double-walled bead, with specific application to islet xenografts. Weber uses a double wall of poly-lysine-alginate layering, and notes the superiority to single-walled microcapsules. The double-walled membrane is formed using polymers with reactive groups, such as polyamino acids including poly-l-lysine and polyethylenimine. Preferably, a poly-l-lysine of 18Kd to 57Kd will be used.

Claims 1-16 and 19-21 have been rejected under 35 U.S.C. §102(e), or alternatively under 35 U.S.C. §103(a), over Lanza. Lanza describes microcapsules and composite microreactors that immunoisolate living cells. Lanza describes coatings preferably formed using a polyamino acid of 15,000 daltons or less. The coating hinders or excludes the passage of molecules having greater than a certain molecular weight. Although the maximum weight of a polymer is preferred, there is no indication that the preferred polymers are of a similar size or chain length, only that they are less than a certain threshold.

Claims 1-17 and 19-21 have been variously rejected under 35 U.S.C. §103(a) Kliment et al., U.S. Patent No. 3,551,556 ("Kliment") in combination with Goosen, Lanza, or Weber. Kliment described slow-release of medicinal preparations using polymeric hydrophilic carriers for biologically active substances. Various polymers, such as a glycol methacrylate and glycol dimethacrylate copolymer, may be used.

None of the cited references discloses or teaches the use of a monodisperse polymer, as the specified citations (25,000 dalton polylysine in Goosen; 18 kD polymer in Weber; and 9.6 kDa polylysine material in Lanza) do not inherently and unambiguously refer to a monodisperse polymer. As described above, one of skill in the art understands that a 25,000 dalton polymer is actually a polymer composition including polymers having a range of molecular weights, with an

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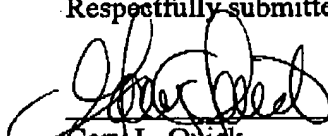Page   : 8 of 8

average molecular weight of 25,000 daltons. The same interpretation holds for the other

molecular weight polymers of the other references. More than this description is required for a

monodisperse polymer, which requires specialized conditions to produce, and will be clearly

characterized or described as monodisperse.

Kliment, discussing polymeric carriers, also does not teach or suggest the use of a

monodisperse polymer, and therefore does not make up for the deficiencies of Goosen, Weber,

or Lanza.

In contrast to the references, claim 1 recites a "coating comprising a monodisperse

polymer." As none of the references teaches, describes, or suggests the use of a monodisperse

polymer, claim 1, and all dependent claims 2-21, are both novel and non-obvious over the cited

references, whether taken alone or in combination, and all rejections should be withdrawn.

No fees are believed to be due. Please apply any other charges or credits to deposit

account 06-1050.

Respectfully submitted,

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Polymer

From Wikipedia, the free encyclopedia

Polymer is a term used to describe molecules consisting of structural units and a large number of repeating units connected by covalent chemical bonds. The term is derived from the Greek words: *polys* meaning *many*, and *meros* meaning *parts* [1] (http://www.etymonline.com/index.php?l=p&p=23). The key feature that distinguishes polymers from other molecules is the repetition of many identical, similar, or complementary molecular subunits in these chains. These subunits, the monomers, are small molecules of low to moderate molecular weight, and are linked to each other during a chemical reaction called polymerization.

Instead of being identical, similar monomers can have various chemical substituents. The differences between monomers can affect properties such as solubility, flexibility, and strength. In proteins, these differences give the polymer the ability to adopt a biologically-active conformation in preference to others. (See self-assembly.) Identical monomers with nonreactive side groups result in a polymer chain that will tend to adopt a random coil conformation, as described by an ideal chain mathematical model. Although most polymers are organic, with carbon-based monomers, there are also inorganic polymers; for example, the silicones, with a backbone of alternating silicon and oxygen atoms and polyphosphazenes.

Contents

Polymer nomenclature

Polymers are typically classified according to four main groups:

- thermoplastics (linear or branched chains)
- thermosets (crosslinked chains)
- elastomers
- Coordination polymers

The term polymer a large, diverse group of molecules, including substances from proteins to stiff, high-strength Kevlar fibres. For example, the formation of polyethene (also called polyethylene) involves thousands of ethene molecules bonded together to form a straight (or branched) chain of repeating $-CH_2-CH_2-$ units (with a $-CH_3$ at each terminal):
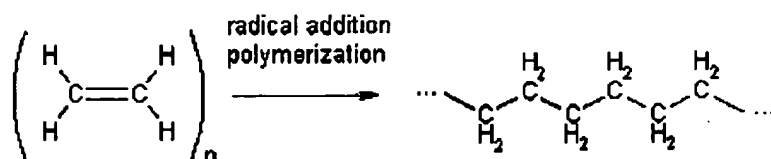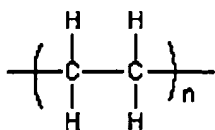

Fig 1: The polymerisation of ethene in to poly(ethene)

Polymers are often named in terms of the monomer from which they are made. Because it is synthesized from ethene in a process during which all the double bonds in the vinyl monomers are lost, polyethene has the unsaturated structure:

$$\left(\begin{array}{cc} \overset{\displaystyle H}{\underset{\displaystyle H}{|}} & \overset{\displaystyle H}{\underset{\displaystyle H}{|}} \\ C - C \end{array}\right)_n$$

Proteins are polymers of amino acids. Typically, hundreds of the (nominally) twenty different amino acid monomers make up a protein chain, and the sequence of monomers determines its shape and biological function. (There are also shorter oligopeptides which function as hormones.) But there are active regions, surrounded by, as is believed now (Aug 2003), structural regions, whose sole role is to expose the active regions. (There may be more than one on a given protein.) So the exact sequence of amino acids in certain parts of the chains can vary from species to species, and even given mutations within a species, so long as the active sites are properly accessible. Also, whereas the formation of polyethylene occurs spontaneously under the right conditions, the synthesis of biopolymers such as proteins and nucleic acids requires the help of enzyme catalysts, substances that facilitate and accelerate reactions. Unlike synthetic polymers, these biopolymers have exact sequences and lengths. (This does not include the carbohydrates.) Since the 1950s, catalysts have also revolutionised the development of synthetic polymers. By allowing more careful control over polymerization reactions, polymers with new properties, such as the ability to emit coloured light, have been manufactured.

Physical properties of polymers

Physical properties of polymers include

- degree of polymerization,
- molar mass distribution, Because synthetic polymer formation is governed by random assembly from the constituent monomers, polymer chains within a solution or substance are generally not of equal length. This is unlike basic, smaller molecules in which every atom is stoichiometrically accounted for, and each molecule has a set molecular mass. An ensemble of differing chain lengths, often obeying a normal (Gaussian) distribution, occurs because polymer chains terminate during polymerization after random amounts of chain lengthening (propagation).
- crystallinity, as well as the thermal phase transitions:
  - T_g, glass transition temperature
  - T_m, melting point (for thermoplastics).
- Branching During the propagation of polymer chains, branching can occur. In free-radical polymerization, this occurs when a chain curls back and bonds to an earlier part of the chain. When this curl breaks, it leaves small chains sprouting from the main carbon backbone. Branched carbon chains cannot line up as close to each other as unbranched chains can. This causes less contact between atoms of different chains, and fewer opportunities for induced or permanent dipoles to occur. A low density results from the chains being further apart. Lower melting points and tensile strengths are evident, because the intermolecular bonds are weaker and require less energy to break. Besides branching, polymers can have other topologies: linear, network (cross-linked 3D structure), IPN (integrated polymer network), comb, or star as well as dendrimer and hyperbranched structures.
- Stereoregularity or tacticity describes the isomeric arrangement of functional groups on the backbone of carbon chains.

Constitution of polymers

Copolymerization with two or more different monomers results in chains with varied properties. There are twenty amino acid monomers whose sequence results in different shapes and functions of protein chains. Copolymerising ethene with small amounts of 1-hexene (or 4-methyl-1-pentene) is one way to form linear low-density polyethene (LLDPE). (See polyethylene.) The C_4 branches resulting from the hexene lower the density and prevent large crystalline regions from forming within the polymer, as they do in HDPE. This means that LLDPE can withstand strong tearing forces while maintaining flexibility.

A block copolymer is formed when the reaction is carried out in a stepwise manner, leading to a structure with long sequences or blocks of one monomer alternating with long sequences of the other. There are also graft copolymers, in which entire chains of one kind (e.g., polystyrene) are made to grow out of the sides of chains of another kind (e.g.,

polybutadiene), resulting in a product that is less brittle and more impact-resistant. Thus, block and graft copolymers can combine the useful properties of both constituents and often behave as quasi-two-phase systems.

The following is an example of step-growth polymerization, or condensation polymerization, in which a molecule of water is given off and nylon is formed. The properties of the nylon are determined by the R and R' groups in the monomers used.
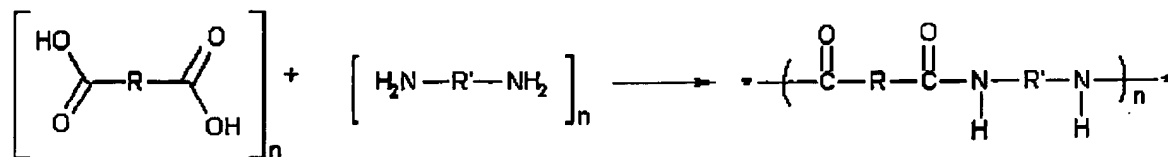
The first commercially successful, completely synthetic polymer was nylon 6,6, with alkane chains R = 4C (adipic acid) and R' = 6C (hexamethylene diamine). Including the two carboxyl carbons, each monomer donates 6 carbons; hence the name. In naming nylons, the number of carbons from the diamine is given first and the number from the diacid second. Kevlar is an aromatic nylon in which both R and R' are benzene rings.

Copolymers illustrate the point that the *repeating unit* in a polymer, such as a nylon, polyester or polyurethane, is often made up of two (or more) monomers.

Chemical properties of polymers

The attractive forces between polymer chains play a large part in determining a polymer's properties. Because polymer chains are so long, these interchain forces are amplified far beyond the attractions between conventional molecules. Also, longer chains are more *amorphous* (randomly oriented). Polymers can be visualised as tangled spaghetti chains - pulling any one spaghetti strand out is a lot harder the more tangled the chains are. These stronger forces typically result in high tensile strength and melting points.

The intermolecular forces in polymers are determined by dipoles in the monomer units. Polymers containing amide groups can form hydrogen bonds between adjacent chains; the positive hydrogen atoms in N-H groups of one chain are strongly attracted to the oxygen atoms in C=O groups on another. These strong hydrogen bonds result in, for example, the high tensile strength and melting point of kevlar. Polyesters have dipole-dipole bonding between the oxygen atoms in C=O groups and the hydrogen atoms in H-C groups. Dipole bonding is not as strong as hydrogen bonding, so ethene's melting point and strength are lower than Kevlar's, but polyesters have greater flexibility.

Ethene, however, has no permanent dipole. The attractive forces between polyethene chains arise from weak van der Waals forces. Molecules can be thought of as being surrounded by a cloud of negative electrons. As two polymer chains approach, their electron clouds repel one another. This has the effect of lowering the electron density on one side of a polymer chain, creating a slight positive dipole on this side. This charge is enough to actually attract the second polymer chain. Van der Waals forces are quite weak, however, so polyethene melts at low temperatures.

Polymer characterization

The characterization of a polymer requires several parameters which need to be specified. This is because a polymer actually consists of a statistical distribution of chains of varying lengths, and each chain consists of monomer residues which affect its properties.

A variety of lab techniques are used to determine the properties of polymers. Techniques such as wide angle X-ray scattering, small angle X-ray scattering, and small angle neutron scattering are used to determine the crystalline structure of polymers. Gel permeation chromatography is used to determine the number average molecular weight, weight average molecular weight, and polydispersity. FTIR, Raman and NMR can be used to determine composition. Thermal properties such as the glass transition temperature and melting point can be determined by differential scanning calorimetry and

dynamic mechanical analysis. Pyrolysis followed by analysis of the fragments is one more technique for determining the possible structure of the polymer.

Polymer known as polymer substrate is used for everyday banknotes in Australia, Romania, Papua New Guinea, Samoa, Zambia, Vietnam, New Zealand and a few others, and the material is also used in commemorative notes in some other countries. The process of polymer substrate creation was developed by the Australia CSIRO.

See also

- Electroactive polymers
- Polymer chemistry
- Polymerization
- Polymer physics
- Important publications in polymer chemistry